REMARKS/ARGUMENTS

Claims 122-126 and 129-131 are pending in this application. The rejections to the presently pending claims are respectfully traversed.

Claim Rejections – 35 U.S.C. §101 and §112, First Paragraph

Claims 122-126 and 129-131 are rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility." (Page 2 of the instant Final Office Action). Claims 122-126 and 129-131 are further rejected under 35 U.S.C. §112, first paragraph, allegedly "since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention." (Page 3 of the instant Final Office Action).

Applicants maintain for the reasons previously set forth in earlier responses that utility of the claimed polypeptides has been achieved. Applicants remarks/arguments in the Preliminary Amendments filed on October 2, 2007 and July 5, 2006, as well as the Appeal Brief filed December 22, 2005, are hereby incorporated by reference in their entirety. Accordingly, withdrawal of the utility and enablement rejections under 35 U.S.C. §101 and §112, first paragraph, are respectfully requested.

Claim Rejections Under 35 U.S.C. §103

Claims 122-126 and 129-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over clone H74302 isolated by Hillier *et al.* (1995) in view of Sibson, WO94/01548. Applicants respectfully traverse and request reconsideration of this rejection in view of the arguments below.

The Examiner asserts that "the two sequences are one, and therefore cannot differ." (Page 6 of the instant Final Office Action).

As disclosed in the instant specification, "In light of an observed sequence homology between the DNA56418 consensus sequence and an EST sequence encompassed within the MercK EST clone no. H74302, the Merck EST clone H74302 was purchased and the cDNA insert was obtained and sequenced." (page 454, lines 34-36) The subsequent sequence analysis carried out by Applicants revealed that the sequence disclosed in the GenBank submission for

H74302 was incomplete and fraught with errors. Through the efforts of the Applicants, "It was found that this insert encoded a full-length protein." (page 454, line 36 of the instant specification). The validated DNA sequence obtained by Applicants was designated as encoding the PRO809 polypeptide (SEQ ID NO:222) and the translated amino acid is represented by SEQ ID NO:223. Applicants submit that the instantly claimed polypeptide sequence of PRO809 could not have been derived from the Wash U-Merck EST H74302 sequence alone, without significant work by the Applicants which would contribute towards "conception, completion and operation" of the invention.

Applicants point out that the GenBank sequence entry of the Wash U-Merck EST clone H74302 discloses a truncated DNA sequence that only overlaps with approximately 58% of the DNA encoding PRO809 (SEQ ID NO: 222; 582 out of 992 bases). Further, as illustrated in the sequence alignment previously made of record between SEQ ID NO:222 and H74302, there is only an 89.5% similarity within the overlapping region between the two sequences. Importantly, the sequence differences between H74302 and SEQ ID NO:222 prevent the identification of the open reading frame encoding PRO809 within H74302. As discussed in the Preliminary Amendment of October 2, 2007, even if one skilled in the are had intended to use the Wash U-Merck EST H74302 sequence as a coding sequence, it would have encoded for a different polypeptide from that of PRO809 (SEQ ID NO: 223). This is evident from looking at all 6 possible reading frames and the alignment enclosed in the IDS of October 2, 2007 between the instantly claimed PRO809 polypeptide and the putative translated Wash U-Merck EST H74302 polypeptide sequence, using the longest open reading frame that bears any similarity to the PRO908 polypeptide sequence. The longest possible polypeptide to be translated from the H74302 sequence would produce a smaller protein sequence with 199 amino acids compared to that of PRO809 polypeptide with 265 amino acids. The difficulty of identifying open reading frames in the H74302 sequence was made worse by the numerous sequencing errors that gave ambiguous base identities (n) and subsequently undeterminable amino acid designations (X). However, the BLAST protein sequence alignments show a minimal sequence similarity of only 16 amino acids between PRO809 polypeptide and Wash U-Merck EST H74302 putative polypeptide sequence (made of record in the IDS of October 2, 2007).

Further, Hillier *et al.*, did not possess or reduce to practice the "complete" polypeptide sequence identical to the instantly claimed PRO809 polypeptide of SEQ ID NO: 223, nor did they teach or disclose how to obtain the polypeptide from the EST clone. One of skill in the art would not have been able to make a polypeptide of SEQ ID NO: 223 without first having realized that Wash U-Merck EST H74302 was part of a coding sequence, an act which would have required additional knowledge about the protein sequence to be used for the DNA extension, like prior knowledge of PRO809's extracellular domain, for instance. Such knowledge was not disclosed or even suggested by the teachings of Hiller et al., (who did not disclose or reduce to practice the encoded polypeptide) around the effective filing date of the instant application. By merely looking at the Wash U-Merck EST H74302 DNA sequence, one would not know whether the sequence would code for the PRO809 polypeptide, or even a part of the protein.

Taken together, Applicants submit that the instantly claimed polypeptide sequence of PRO809 could not have been derived from the Wash U-Merck EST H74302 sequence alone, without significant work by the Applicants which would contribute towards "conception, completion and operation" of the invention. Applicants used their own knowledge (clustering analysis, extension of DNA sequences and PCR-based cDNA library screening to obtain the full-length nucleic acid sequence encoding for the PRO809 polypeptide, etc.) and were the first to reduce to practice the PRO809 polypeptide of SEQ ID NO: 223. Further, even if the Wash U-Merck EST H74302 polypeptide sequence were supposedly reduced to practice, the sequence does not encode for the PRO809 polypeptide nor a polypeptide having at least 95% amino acid sequence identity to the PRO809 polypeptide of SEQ ID NO: 223. Accordingly, Hillier et al. do not teach or anticipate the polypeptides of Claims 122-126 and 129-131.

Further, the secondary reference Sibson et al. also does not cure the deficiencies of Hillier. Therefore, this §103(a) rejection falls as neither reference teaches or anticipate the instantly claimed polypeptide.

Accordingly, neither of the cited references teach or anticipate the instant invention and thus, this rejection under 35 U.S.C. §103(a) should be withdrawn..

CONCLUSION

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **07-1700** (referencing Attorney's Docket No. **123851-181895 (39780-2730 P1C15)**.

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: June 16, 2008

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